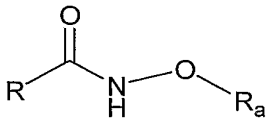
WHAT IS CLAIMED IS:

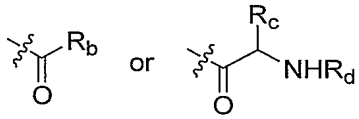
1. A prodrug of a hydroxamic acid derivative histone deacetylase (HDAC) inhibitor, represented by the structure of formula 1:



(1)

wherein R is a residue of a hydroxamic acid derivative histone deacetylase inhibitor; and

$R_a$ is represented by the structure:



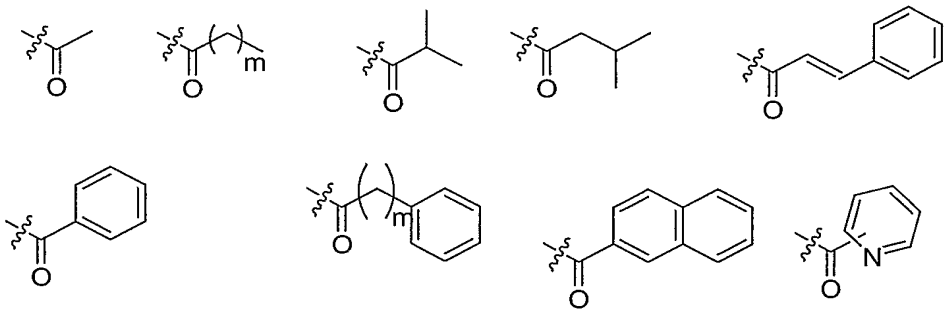
wherein $R_b$ and $R_c$ are independently of each other a hydrogen or an unsubstituted or substituted alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl, heteroaryl, alkylaryl, alkylcycloalkyl, alkylheterocyclyl, alkylheteroaryl or an amino acid residue; and

$R_d$ is hydrogen or an amino protecting group;

or a pharmaceutically acceptable salt, hydrate, solvate, polymorph or any combination thereof.

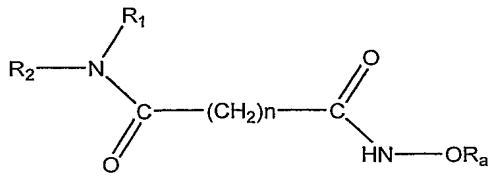
2. The prodrug according to claim 1, wherein $R_b$ and $R_c$ are independently of each other a hydrogen, methyl, ethyl, isopropyl, butyl, isobutyl, sec-butyl, t-butyl, phenyl, benzyl, alkylphenyl, napththyl or pyridyl.

3. The prodrug according to claim 1, wherein $R_a$ is selected from the group consisting of:



and wherein m is an integer of 1 to 10.

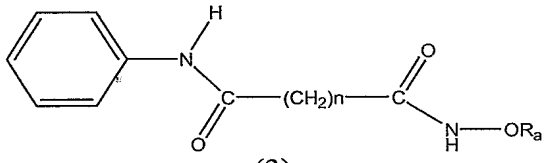
4. The prodrug according to claim 1, represented by the structure:



(2)

wherein each of $R_1$ and $R_2$ are independently the same as or different from each other and are a hydrogen atom, a hydroxyl group, a substituted or unsubstituted, branched or unbranched alkyl, alkenyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, arylalkyloxy, aryloxy, or pyridine group, or $R_1$ and $R_2$ are bonded together to form a nitrogen containing heterocyclic ring optionally containing one or more additional heteroatoms, and n is an integer of 4 to 8.

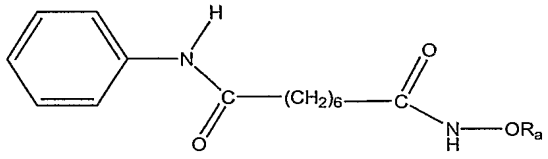
5. The prodrug according to claim 1, represented by the structure:



(3)

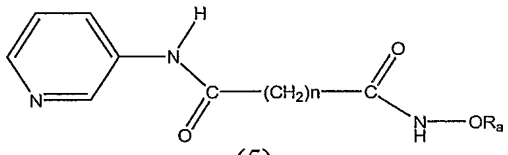
wherein n is an integer of 4 to 8.

6. The prodrug according to claim 1, represented by the structure:



(4)

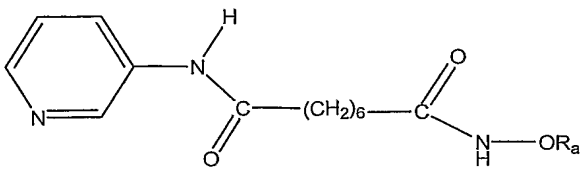
7. The prodrug according to claim 1, represented by the structure:



(5)

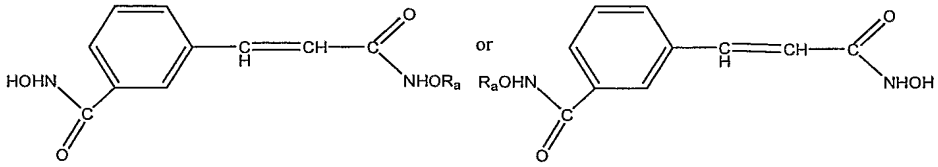
wherein n is an integer from about 4 to about 8.

8. The prodrug according to claim 1, represented by the structure:



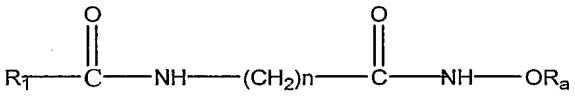
(6)

9. The prodrug according to claim 1, represented by the structure:



(9) (10)

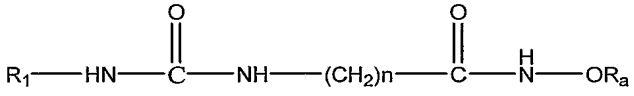
10. The prodrug according to claim 1, represented by the structure:



(11)

wherein $R_1$ is a substituted or unsubstituted phenyl, piperidino, thiazolyl, 2-pyridinyl, 3- pyridinyl or 4-pyridinyl and n is an integer of 4 to 8.

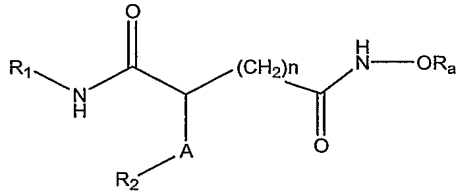
11. The prodrug according to claim 1, represented by the structure:



(12)

wherein $R_1$ is a substituted or unsubstituted phenyl, piperidino, thiazolyl, 2-pyridinyl, 3- pyridinyl or 4-pyridinyl and n is an integer of 4 to 8.

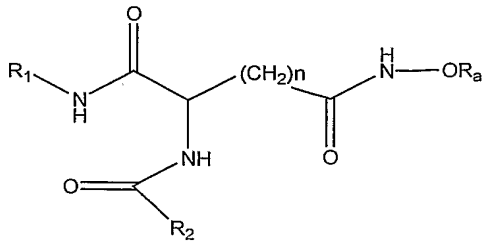
12. The prodrug according to claim 1, represented by the structure:



(13)

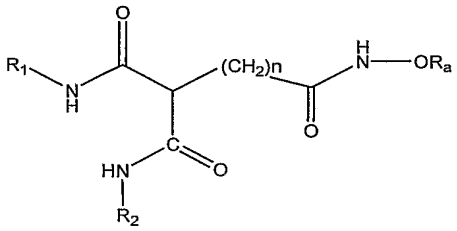
wherein A is an amide moiety, $R_1$ and $R_2$ are each selected from substituted or unsubstituted aryl, arylalkyl, naphthyl, cycloalkyl, cycloalkylamino, pyridineamino, piperidino, 9-purine-6-amino, thiazoleamino, hydroxyl, branched or unbranched alkyl, alkenyl, alkyloxy, aryloxy, arylalkyloxy, pyridyl, quinolinyl or isoquinolinyl; and n is an integer of 3 to 10.

13. The prodrug according to claim 12, represented by the structure:



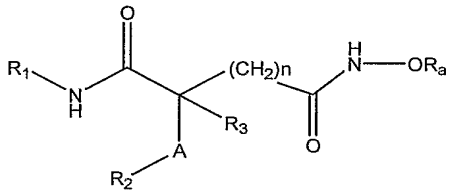
(13a)

14. The prodrug according to claim 12, represented by the structure:



(13b)

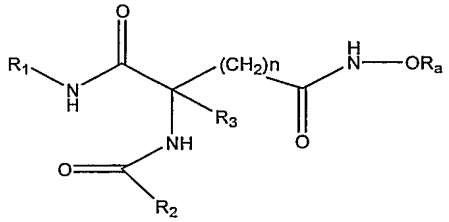
15. The prodrug according to claim 1, represented by the structure:



(14)

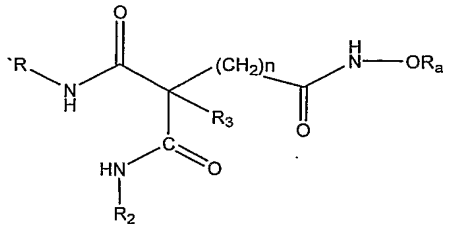
wherein A is an amide moiety, $R_1$ and $R_2$ are each selected from substituted or unsubstituted aryl, arylalkyl, naphthyl, cycloalkyl, cycloalkylamino, pyridineamino, piperidino, 9-purine-6-amino, thiazoleamino, hydroxyl, branched or unbranched alkyl, alkenyl, alkyloxy, aryloxy, arylalkyloxy, pyridyl, quinolinyl or isoquinolinyl; $R_3$ is hydrogen, a halogen, a phenyl or a cycloalkyl moiety and n is an integer of 3 to 10.

16. The prodrug according to claim 15, represented by the structure:



(14a)

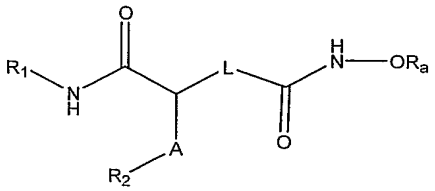
17. The prodrug according to claim 15, represented by the structure:



(14b)

wherein n is an integer from about 3 to 10.

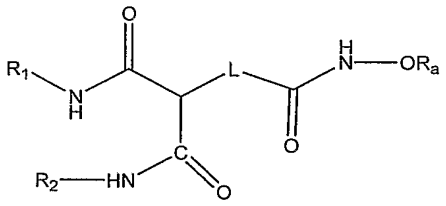
18. The prodrug according to claim 1, represented by the structure:



(15)

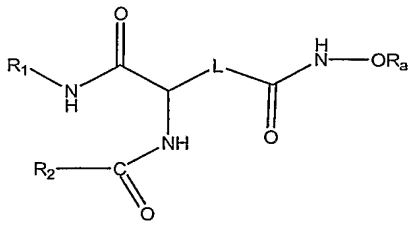
-wherein L is a linker selected from the group consisting of an amide moiety, O-, -S-, -NH-, NR, $-CH_2-$, $-(CH_2)_p-$, -(CH=CH)-, phenylene, cycloalkylene, or any combination thereof wherein R is a substituted or unsubstituted $C_1$-$C_5$ alkyl; and wherein each of $R_1$ and $R_2$ are independently a substituted or unsubstituted aryl, arylalkyl, naphthyl, cycloalkyl, cycloalkylamino, pyridineamino, piperidino, 9-purine-6-amino, thiazoleamino, hydroxyl, branched or unbranched alkyl, alkenyl, alkyloxy, aryloxy, arylalkyloxy, pyridyl, quinolinyl or isoquinolinyl; p is an integer of 0 to 10.

19. The prodrug according to claim 18, represented by the structure:



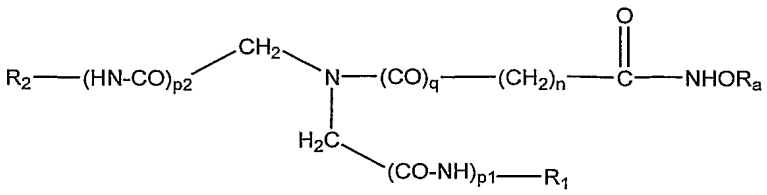
(15a)

20. The prodrug according to claim 18, represented by the structure:



(15b)

21. The prodrug according to claim 1, represented by the structure:



(29)

wherein

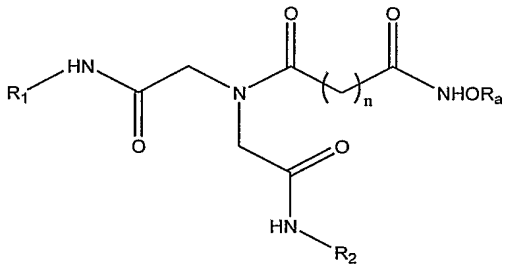
n is 2, 3, 4, 5, 6, 7 or 8;

q is 0 or 1;

$p_1$ and $p_2$ are independently of each other 0 or 1;

$R_1$ and $R_2$ are independently of each other an unsubstituted or substituted aryl, heteroaryl, cycloalkyl, heterocyclyl, alkylaryl, alkylheteroaryl, alkylcycloalkyl or alkylheterocyclyl; or when $p_1$ and $p_2$ are both 0, $R_1$ and $R_2$ together with the $-CH_2$-N-$CH_2$- group to which they are attached can also represent a nitrogen-containing heterocyclic ring; or when at least one of $p_1$ or $p_2$ is not 0, $R_1$ or $R_2$ or both can also represent hydrogen or alkyl.

22. The prodrug according to claim 1, represented by the structure:



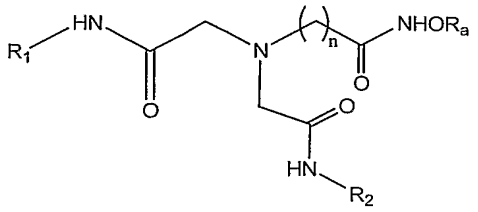
(30)

wherein

n is 2, 3, 4, 5, 6, 7 or 8;

$R_1$ and $R_2$ are independently of each other a hydrogen or an unsubstituted or substituted alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, alkylaryl, alkylheteroaryl, alkylcycloalkyl or alkylheterocyclyl.

23. The prodrug according to claim 1, represented by the structure:



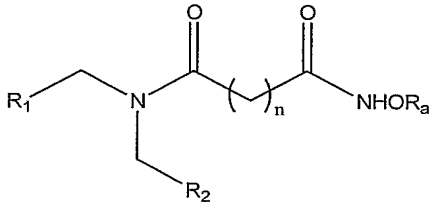
(31)

wherein

n is 2, 3, 4, 5, 6, 7 or 8;

$R_1$ and $R_2$ are independently of each other a hydrogen or an unsubstituted or substituted alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, alkylaryl, alkylheteroaryl, alkylcycloalkyl or alkylheterocyclyl.

24. The prodrug according to claim 1, represented by the structure:



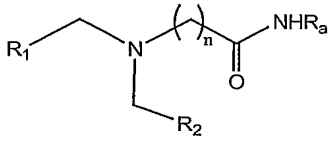
(32)

wherein

n is 2, 3, 4, 5, 6, 7 or 8;

$R_1$ and $R_2$ are independently of each other an unsubstituted or substituted aryl, heteroaryl, cycloalkyl, heterocyclyl, alkylaryl, alkylheteroaryl, alkylcycloalkyl or alkylheterocyclyl; or $R_1$ and $R_2$ together with the $-CH_2-N-CH_2-$ group to which they are attached can also represent a nitrogen-containing heterocyclic ring.

25. The prodrug according to claim 1, represented by the structure:



(33)

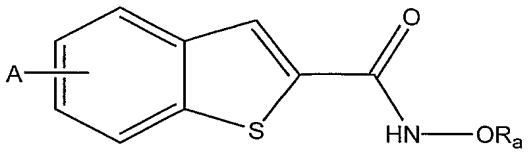
wherein

n is 2, 3, 4, 5, 6, 7 or 8;

$R_1$ and $R_2$ are independently of each other an unsubstituted or substituted aryl, heteroaryl, cycloalkyl, heterocyclyl, alkylaryl, alkylheteroaryl, alkylcycloalkyl or alkylheterocyclyl; or $R_1$ and $R_2$ together with the $-CH_2-$

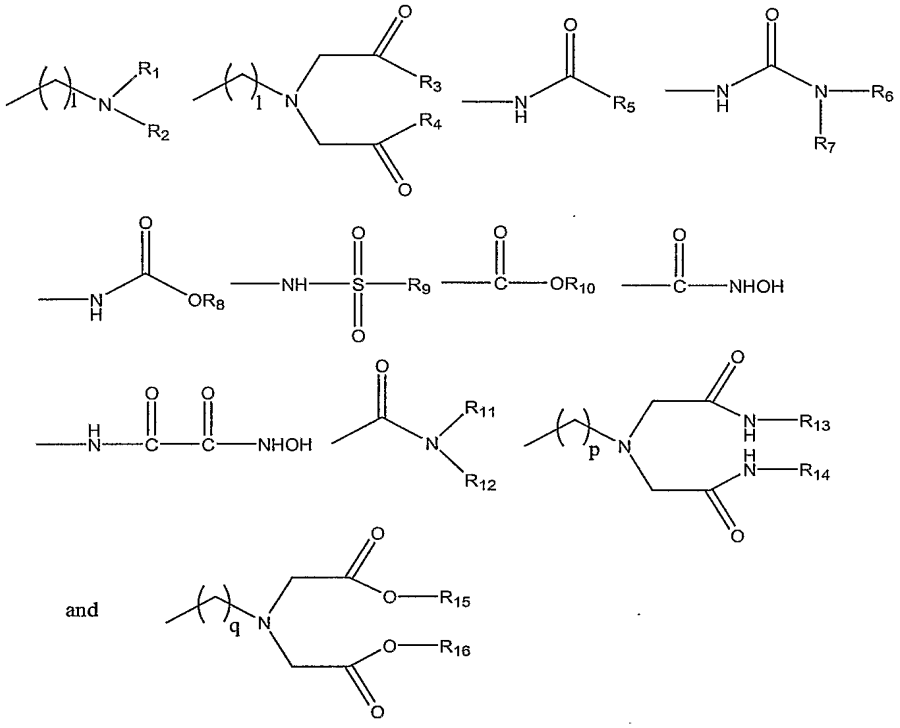
N-$CH_2$- group to which they are attached can also represent a nitrogen-containing heterocyclic ring.

26. The prodrug according to claim 1, represented by the structure:



(34)

wherein A is alkyl, aryl or a group selected from



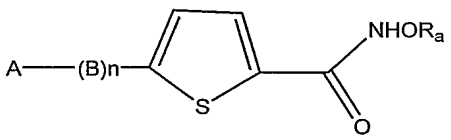
and



wherein $R_1$-$R_{16}$ are independently of each other a hydrogen or an unsubstituted or substituted alkyl, aryl, cycloalkyl, heterocyclyl, alkylaryl, alkylcycloalkyl or alkylheterocyclyl; or one or more of $R_1$ and $R_2$, $R_6$ and $R_7$, and $R_{11}$ and $R_{12}$, together with the nitrogen atom to which they are attached, form a nitrogen-containing heterocyclic ring; and

l, p and q are independently of each other 0, 1 or 2.

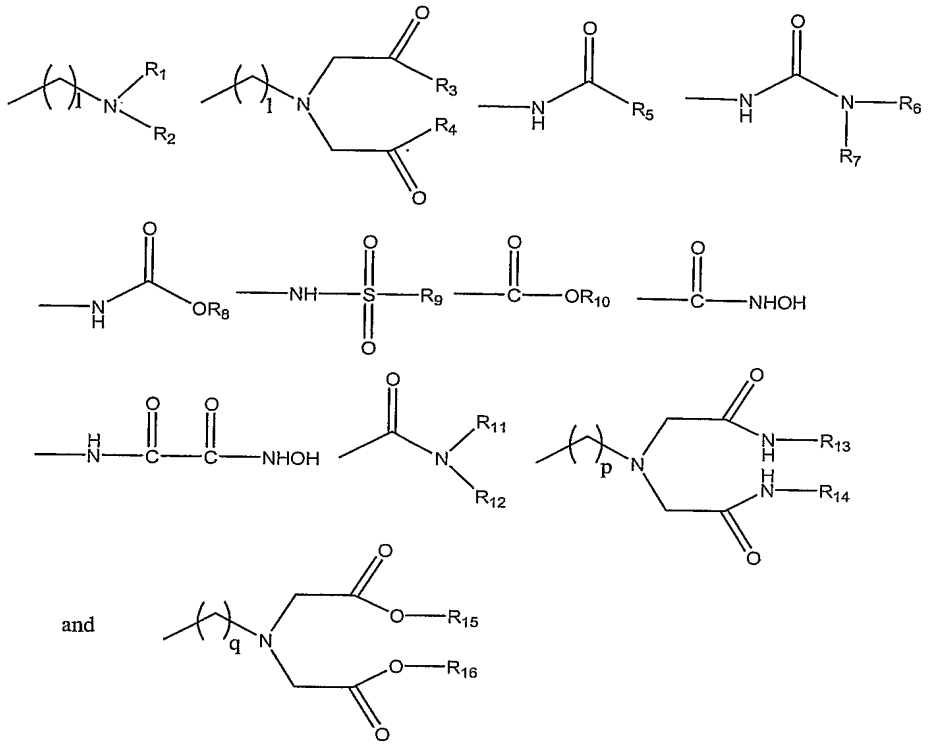
27. The prodrug according to claim 1, represented by the structure:



(36)

wherein

A is alkyl, aryl or a group selected from:

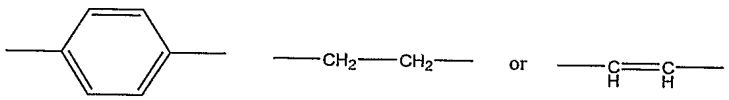


and



wherein $R_1$-$R_{16}$ are independently of each other a hydrogen or an unsubstituted or substituted alkyl, aryl, cycloalkyl, heterocyclyl, alkylaryl, alkylcycloalkyl or alkylheterocyclyl; or one or more of $R_1$ and $R_2$, $R_6$ and $R_7$, and $R_{11}$ and $R_{12}$, together with the nitrogen atom to which they are attached, form a nitrogen-containing heterocyclic ring;

B is



n is 0 or 1; and

l, p and q are independently of each other 0, 1 or 2.

28. A pharmaceutical composition comprising the prodrug of claim 1 or a pharmaceutically acceptable salt or hydrate thereof, and a pharmaceutically acceptable carrier.

29. Use of the prodrug of claim 1 in the manufacture of a medicament for the treatment of cancer.

30. Use of the prodrug of claim 1 in the manufacture of a medicament for the treatment of a thioredoxin (TRX)-mediated disease.

31. Use of the prodrug of claim 1 in the manufacture of a medicament for the treatment of a disease of the central nervous system.

32. Use of the prodrug of claim 1 in the manufacture of a medicament for the treatment of a tumor characterized by proliferation of neoplastic cells.